10. (Amended) A tissue into which the gene encoding the polynucleotide according to Claim 1 is introduced.

11. (Amended) A cell into which the gene encoding the polynucleotide according to Claim 1 is introduced.

12. (Amended) A method of knocking-in a desired gene in a location controlled and/or time-controlled manner; comprising the steps of:

(1) introducing a first gene construct and a second construct into cells, tissues, organs or whole bodies,

wherein the first gene comprises a polynucleotide according to Claim 1 and an inducible promoter for inducing expression of the polynucleotide at a site into which the desired gene is to be knocked-in, in a location-controlled and/or time-controlled manner; and the second gene construct comprises a first loxP sequence, a second loxP sequence located downstream of the first loxP sequence, a second promoter sequence located upstream of the first loxP sequence, and the desired gene located downstream of the second loxP sequence,

(2) expressing a Cre recombinase gene by the inducible promoter in a location-controlled and/or time-controlled manner, and

(3) placing the desired gene under control of the promoter sequence in the second gene construct by means of site specific recombination on the second gene construct by Cre recombinase expressed in step (2), thereby knocking-in the desired gene in a location-controlled manner and/or time-controlled manner.

13. (Amended) A method of knocking-out a desired gene in a location controlled and/or time- specific manner; comprising the steps of:

(1) introducing a first gene construct and a second gene construct into cells tissues organs or whole bodies,

wherein the first gene construct comprises a polynucleotide according to Claim 1 and an inducible promoter for inducing expression of polynucleotide at a site into which the desired gene is to be knocked-out, in a location-controlled and/or time-controlled manner; and the second gene construct comprises a first loxP sequence, a second loxP sequence located downstream of the first loxP sequence, a promoter sequence located upstream or downstream of the first loxP sequence, and the desired gene located downstream of the promoter and the first loxP sequence,

(2) expressing a Cre recombinase gene by the inducible promoter in a location-controlled manner, and

(3) falling off a part or whole of the desired gene from the second gene construct by means of site specific recombination on the second gene construct by Cre recombinase expressed in step (2), thereby knocking-out at least a part or whole of the desired gene, in a location-controlled and/or time-controlled manner.

14. (Amended) The method of claim 12, wherein the desired gene is selected from the group consisting of a xenograft antigen, carcinogenic antigen, and anti antibody-production-associated-molecule antibody.

21. (Amended) A method for treating a disease caused by malfunction of an organ, comprising a step of transplanting ~~the organ according to Claim 18,~~ into an organism.--

Please add the following claims.

--22. (New) The method according to Claim 13, wherein the desired gene is selected from the group consisting of a xenograft antigen, carcinogenic antigen, and anti antibody-

production-associated-molecule antibody.

23. (New) A method for treating a desease caused by malfunction of a tissue, comprising a step of transplanting the tissue according to Claim 19 into an organism.

24. (New) A method for treating a desease caused by malfunction of a cell, comprising a step of transplanting the cell according to Claim 20 into an organism.--

BASIS FOR THE AMENDMENT

Original Claims 7-14 and 21 have been amended to remove multiple dependency. New Claims 22-24 have been added. Support for the additional claims is found in the original Claims 1-21. No matter is believed to be introduced by the amendments to the specification and claims.

REMARKS

Claims 1-24 are active in the present application.

The Office has required restriction in the present application as follows:

Group I:	Claims 1-11, drawn to a modified Cre recombinase gene, a cell comprising said Cre recombinase gene, a tissue, an organ or an animal comprising Cre recombinase gene;
Group II:	Claims 13 and 14, drawn to a method of knocking-out a gene from a transgenic animal;
Group III:	Claims 12, 14, and 15, drawn to a method of knocking-in a gene in a location controlled manner from a cell, and a transgenic knock-in animal;
Group IV:	Claims 16-20, drawn to a transgenic animal from which a second desired gene is knocked-out, and an organ, tissue and cell taken out from the animal;

Group V: Claim 21, drawn to a method for treating a disease.

Applicants have elected Group I, Claims 1-11, with traverse, for further prosecution.

Applicants submit that claims of Groups II-V are directly dependent from the claims of Group I, as such these groups can not be separated.

Further, Applicants wish to note that Group I is directed to a Cre recombinase gene and Groups II and III are directed to the use of this gene. Accordingly, it would be improper to separate these groups.

Applicants respectfully traverse the Restriction Requirement on the grounds that no adequate reasons and/or examples have been provided to support a conclusion of patentable distinctness between the identified groups.

Further, MPEP §803 states as follows:

> If the search and examination of an entire application can be made without serious burden, the Examine must examine it on its merits, even though it includes claims to distinct or independent inventions.

Applicants submit that a search of all claims would not constitute a serious burden on the Office, particularly in view of the fact that Groups II-IV are classified in the same subclass (class 800, subclass 21).

Additionally, MPEP §821.04 states:

> ...if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

Applicants respectfully submit that should the elected group be found allowable, the corresponding non-elected process claims should be rejoined.

Applicants respectfully submit that the above-identified application is now in condition for examination on the merits, and early notice of such action is earnestly solicited.

Respectfully submitted,

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